REMARKS

Claims 1-3 and 39-56 were previously pending in this application. Claims 2, 39-53 and 55 have been cancelled without prejudice to the filing of any appropriate continuation applications. New claims 57-63 are added.

Applicants have amended the claims to more clearly define and distinctly characterize Applicants' novel invention. Specifically, claim 1 was amended to recite a method for diagnosing a precancerous lesion or a cancer in a ***human***, comprising detecting and measuring gene copy number of a WIP1 gene having a nucleotide sequence of ***nucleotides 1-1818*** of SEQ ID NO:1 or of ***nucleotides 1-2973*** of SEQ ID NO:3 in a ***breast tissue*** or ***lung tissue*** sample from the human that is suspected to be precancerous or cancerous, thereby generating data for a test gene copy number; and comparing the test gene copy number to data for a control gene copy number, wherein an amplification of the gene in the breast tissue or lung tissue sample relative to the control indicates the presence of a precancerous lesion or cancer in the human. Support for human can be found at least at paragraph [0016] of the published application, where Applicants teach mammals such as humans. Support for detecting and measuring gene copy number in breast tissue or lung tissue can be found in Applicants specification at least at Table 2 which demonstrates an amplification of WIP1 DNA copy number in breast tumor samples and lung tumor samples (page 16 of the published application). Support for nucleotides 1-1818 of SEQ ID NO:1 and nucleotides 1-2973 of SEQ ID NO:3 can be found at least at Applicants' sequence listing which teaches that SEQ ID NO:1 contains nucleotides 1-1818 and that SEQ ID NO:3 contains nucleotides 1-2973.

New claims 57-63 have been added simply to identify the various ways of determining the gene copy number, an operative element of claim 1. Support for these various detection techniques are elaborated over pages 41 through 43. The addition of these dependent claims do not raise a new issue for consideration. The patentability of these claims follows the patentability of claim 1.

The amendments presented herein add no new matter and do not raise any new issues requiring further search. With the amendment, applicants have reduced the number of pending claims and have narrowed any issues for appeal. Applicants respectfully request entry and

consideration of the foregoing amendments, which are intended to place this case in condition for allowance, or at least in better condition for appeal. Thus, entry of the amendment under Rule 116 is requested.

The Rejections

Claims 1-3 and 39-56 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Claims 1-3 and 39-56 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claims 1-3 and 39-56 stand rejected under 35 U.S.C. § 102(b), as being anticipated by Kallioniemi et al. (1994) *Proc. Natl. Acad. Sci. U.S.A.* 91:2156. Claims 1-3 and 39-56 stand rejected under 35 U.S.C. § 102(b), as being anticipated by Lavi, WO 97/10796. Applicants gratefully acknowledge the withdrawal of the rejection of claims 1-3 under 35 U.S.C. § 112, second paragraph, as being indefinite.

The Pending Claims are Enabled

At page 3, section 4 of the Office Action, claims 1-3 and 39-56 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. The Office Action states that the specification does not reasonably provide enablement for diagnosing *any* cancer in *any* mammal by measuring and detecting *any* amplification in the gene copy number of *any* "WIP1" gene in *any* biological subject that is suspected to be cancerous. The Office Action states that the guidance provided by the specification does not provide a predictable correlation between amplification of the claimed WIP1 sequences and *any* type of cancer. The Office Action notes that the specification teaches that sequence identity to the claimed sequences may be determined over a comparison window, but that the specification does not teach which sequences within the claimed sequences can be used for the comparison window. The Office Action further states that the specification does not teach a predictable association between amplification of the WIP1 genomic gene and a representative amount of different cancers. Applicants respectfully traverse this rejection based on the amended claims now presented.

Without acquiescing to the rejection, Applicants respectfully submit that claim 1 has been amended to recite a method for diagnosing a precancerous lesion or a cancer in a ***human***, comprising detecting and measuring gene copy number of a WIP1 gene having a nucleotide

sequence of ***nucleotides 1-1818*** of ***SEQ ID NO:1*** or of ***nucleotides 1-2973*** of ***SEQ ID NO:3*** in a ***breast tissue or lung tissue*** sample from the human that is suspected to be precancerous or cancerous, thereby generating data for a test gene copy number, and comparing the test gene copy number to data for a control gene copy number, wherein an amplification of the gene in the breast tissue or lung tissue sample relative to the control indicates the presence of a precancerous lesion or cancer in the human. Accordingly, the pending claims recite a specific sequence that may be used for comparison, and that the precancerous lesion or cancer is diagnosed in specific tissue samples: human breast tissue or human lung tissue.

Applicants respectfully submit that the pending specification adequately teaches one of skill in the art how to make and use the claimed invention without undue experimentation. Applicants note that the level of skill in the art has been deemed to be high (page 9 of the Office Action).

Applicants' specification teaches that the term cancer refers to the presence of cells possessing characteristics typical of cancer-causing cells such as uncontrolled proliferation, loss of specialized functions, immortality, significant metastatic potential, rapid growth, rapid proliferation, and the like (paragraph [0050] of the published application). Applicants' specification teaches that the term precancerous refers to tissues having characteristics relating to changes that may lead to malignancy or cancer, such as adenomatous growths in breast tissue or lung tissue as well as abnormal neoplastic syndromes (paragraph [0053] of the published application).

Applicants' specification teaches that the claimed tissue is one that contains or is suspected of containing nucleic acids or polypeptides of WIP1 (paragraph [0091] of the published application). Further, Applicants' specification specifically teaches that increased WIP1 gene copy number as well as RNA overexpression was observed in both breast tumor samples and lung tumor samples using Taqman and RT-Taqman, respectively (Table 2, page 16 of the published application).

Applicants' specification sets forth the nucleic acid sequence of nucleotides 1-1818 of SEQ ID NO:1 and nucleotides 1-2973 of SEQ ID NO:3 (pages 27 and 14 of the published application, respectively, and Applicants' sequence listing). Further, the Office Action states

"...***with the exception of SEQ ID NO:1 or 3***, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides..." (Office Action, page 15, emphasis added).

Finally, Applicants' specification teaches a variety of standard techniques that may be used to determine WIP1 gene copy number, including, but not limited to, Southern blotting, fluorescence *in situ* hybridization, comparative genomic hybridization, PCR, ligase chain reaction, microarray-based platforms and the like (paragraphs [0152] – [0160]).

Based on Applicants' teachings described above and the high level of skill in the art, one of skill in the art would readily be able to ascertain whether a WIP1 gene copy having the claimed sequence is increased in a breast tissue or lung tissue sample using only routine methods. Nothing more is necessary to enable the claimed methods. For at least these reasons, Applicants' specification, coupled with the level of skill in the art, enables a person of skill in the art to make and/or use the claimed invention. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1-3 and 39-56 under 35 U.S.C. § 112, first paragraph, as lacking enablement.

The Specification Provides Adequate Written Description for the Pending Claims

At page 13, section 6 of the Office Action, claims 1-3 and 39-56 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office Action asserts that, based on the broad definition of WIP1 genes encompassed by the sequences of 70-100% identity, which includes sequences that may be completely unrelated to WIP1 based on the comparison window chosen for determining sequence identity, and sequences comprising portions of SEQ ID NO:1 or 3, the large genus of WIP1 genes recited in the claims encompasses structurally and functionally distinct molecules, which have not been taught or described in the specification, whose amplification would not necessarily be expected to be associated with cancer. The Office Action also states that the specification provides no correlation between the structure of potential WIP1 homologs or portions of WIP1 and function either of encoded protein or functional association to cancer in general, or any particular type of cancer. The Office Action also states that the art does not support a predictable relationship between genes with homology to human WIP1 and gene copy number amplification in cancer.

The Office Action maintains that the disclosure of SEQ ID NO:1 and 3 is not representative of the broad variable genus of polynucleotides encompassed by the claims. Applicants respectfully traverse this rejection based on the amended claims now presented.

Applicants respectfully submit that the specification more than adequately describes the claimed methods with reasonable clarity to one of skill in the art. As described above, Applicants teach specific samples, i.e., human breast tissue samples and lung tissue samples, that may be used in the claimed methods; teach the specific identity of a WIP1 gene, i.e., a gene having a nucleotide sequence of nucleotides 1-1818 of SEQ ID NO:1 or nucleotides 1-2973 of SEQ ID NO:3; and describe a variety of methods in which a gene copy number may be detected and measured. Thus, one of skill in the art would recognize that the specification adequately describes the claimed method.

When read as a whole, taking into account the high level of skill of persons in the art at the filing date of the application, this specification indicates to those skilled in the art that Applicants had possession of the claimed subject matter at the time of filing. Accordingly, Applicants request that the rejection of claims 1-3 and 39-56 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement be reconsidered and withdrawn.

The Pending Claims are Novel Over Kallioniemi et al.

At page 18, section 8 of the instant Office Action, claims 1-3 and 39-56 stand rejected under 35 U.S.C. 102(b) as being anticipated by Kallioniemi et al. (1994) *Proc. Natl. Acad. Sci. U.S.A.* 91:2156, as defined by Wu et al. (2001) *Cancer Res.* 61:4951. Applicants respectfully traverse this rejection based on the amended claims now presented.

Applicants respectfully submit that Kallioniemi et al. provides no specific teaching that ***any*** WIP1 gene, let alone a WIP1 gene having a specific nucleotide sequence of ***nucleotides 1-1818 of SEQ ID NO:1*** or of ***nucleotides 1-2973 of SEQ ID NO:3*** as claimed by Applicants, has any association with breast cancer. Kallioniemi et al. merely teaches that the ***entire chromosomal region 17q22-q24*** is amplified in certain breast cancer cell lines and primary tumors (abstract).

Wu et al. fails to cure the deficiencies of Kallioniemi et al. The Office Action asserts that Wu et al., which has a publication date that is after Applicants' priority date, was properly used to define that the human WIP1 gene is located in the 17q22-23 region of chromosome 17. Applicants respectfully disagree. The Office Action asserts that MPEP 2112, section 2 states that "[t]here is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of the invention, but only that the subject matter ***is in fact inherent*** in the prior art reference" (Office Action, page 20, emphasis added). However, Wu et al. does ***not*** prove that Kallioniemi et al. ***inherently*** teaches amplification of nucleotides 1-1818 of SEQ ID NO:1 or of nucleotides 1-2973 of SEQ ID NO:3 of WIP1. In fact, based on the teachings of Wu et al., one of skill in the art would understand that ***any one of at least 20 genes*** which were amplified in the 17q22-***23*** region of chromosome 17 in breast cancer cell lines and tumors could have been responsible for the observed amplification of 17q22-24 region of chromosome 17 as reported by Kallioniemi et al. In fact, Kallioniemi et al. teaches that candidate genes in this region include HOX2, NGFR, PRKCA, HLR1 and NMEI (page 2159, right column). Kallioniemi et al. fails to identify WIP1 as a possible candidate. Further, Wu et al. does not analyze the 17q***24*** region of chromosome 17, which may contain additional genes which could have been responsible for the regional amplification observed by Kallioniemi et al. It simply does not follow that Kallioniemi et al. inherently teaches amplification of any WIP1 sequence (e.g., specific polymorphisms), let alone Applicants' claimed nucleotide sequence.

The Office Action notes that the language "...a nucleotide sequence of SEQ ID NO..." in claims 45-47 and 54-56 as being ***any sequence within*** the ***recited sequence***. The Office Action states that, given that there is no definition of the sequences within the claimed sequences that can be used for the comparison window, it is highly likely that the WIP1 gene in the chromosome 17 region found amplified by Kallioniemi would contain ***regions*** of sequence in comparison windows that are ***identical to that of SEQ ID NO:1 or 3***. The Office Action maintains that Kallioniemi as defined by Wu teaches a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region, which contains the human WIP1 gene of at least 99.7% and ***likely 100% identity*** in ***certain regions*** to SEQ ID NO:1 and 3, in several human primary breast tumors and breast cancer cell lines.

Applicants respectfully disagree. For at least the reasons set forth above, Applicants submit that it is does not follow that WIP1 was ***necessarily responsible*** for the observed copy number increase of the 17q22-24 region of chromosome 17 as reported by Kallioniemi. However, in order to expedite prosecution and without acquiescing to the rejection, Applicants note that the amended claims are directed in part to a method for diagnosing a precancerous lesion or a cancer comprising detecting and measuring gene copy number of a WIP1 gene having a nucleotide sequence of ***nucleotides 1-1818 of SEQ ID NO:1*** or of ***nucleotides 1-2973 of SEQ ID NO:3***. Thus, the pending claims define the ***entire*** SEQ ID NO:1 or SEQ ID NO:3 sequence, i.e., nucleotides 1-1818 or 1-2973, respectively, that can be used for a comparison window with the art. Accordingly, Kallioniemi et al. fails to teach or suggest the claimed methods.

For at least these reasons, Applicants respectfully request that the rejection of claims 1-3 and 39-56 under 35 U.S.C. § 102(b) as being anticipated by Kallioniemi et al. be reconsidered and withdrawn.

The Pending Claims are Novel Over Lavi

At page 22, section 10 of the Office Action, claims 1-3 and 39-56 stand rejected under 35 U.S.C. 102(b) as being anticipated by Lavi, WO 97/10796. Applicants respectfully traverse this rejection based on the amended claims now presented.

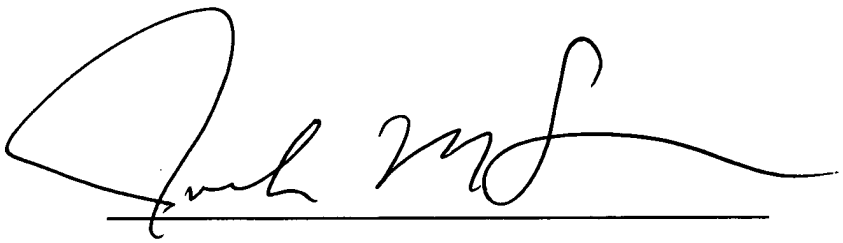
The Lavi reference fails to teach or suggest the claimed invention. The Office Action states that as Fiscella teaches that the PP2Calpha gene has ***regions*** of greater than 70% sequence identity to human WIP1, PP2Calpha is highly likely to have ***regions of 100% identity*** in ***certain comparison windows***. The Office Action concludes that PP2Calpha, the gene detected in the method of detecting cancer taught by Levi, is a sequence having at least 70% identity to SEQ ID NO:1 or 3 as defined by "percentage of sequence identity" in the specification. Applicants note, however, that WIP1 cDNA shows ***limited similarity*** to other PP2C phosphatases ***except*** in ***three conserved regions***, which only have ***50-77% sequence identity*** within ***the conserved regions*** (Fiscella et al. (1997 *Proc. Natl. Acad. Sci. USA* 94:6048, page 6050, first partial paragraph and Figure 1). Applicants respectfully submit that the Lavi reference neither teaches nor suggests a method of diagnosing a precancerous lesion or a cancer by detecting and measuring gene copy

number of a WIP1 gene or a method of diagnosing a precancerous lesion or a cancer by detecting and measuring gene copy number of a WIP1 gene having a nucleotide sequence of ***nucleotides 1-1818 of SEQ ID NO:1*** or of ***nucleotides 1-2973 of SEQ ID NO:3***. Accordingly, Applicants respectfully request that the rejection of claims 1-3 and 39-56 under 35 U.S.C. § 102(b) as being anticipated by Lavi be reconsidered and withdrawn.

Conclusion

Having addressed all outstanding issues, Applicants respectfully request entry and consideration of the foregoing amendments and reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,



Date: May 10, 2006

Joseph M. Skerpon
Registration No. 29,864

BANNER & WITCOFF, LTD.
1001 G Street, N.W.
Washington, D.C. 20001
Telephone: (202) 824-3000